

Amendments to the Drawings:

Please replace the original 26 sheets of drawings comprising Figures 1-21 with the enclosed set of 48 replacement drawing sheets which also comprise Figures 1-21. The Figures have been amended to conform with standards for font size and clarity drawings as defined under 37 C.F.R. 1.84 (l) and 1.84 (p).

Attachment: 48 Replacement Sheets

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ATGGCCCAAGCCCTGCCCTGGCTCCTGCTGTGGATGGGCGCGGGAG
TGCTGCCTGCCCACGGCACCCAGCACGGCATCCGGCTGCCCCTGCG
CAGCGGCCTGGGGGGCGCCCCCTGGGGCTGCGGCTGCCCCGGGA
GACCGACGAAGAGCCCGAGGAGCCCGGCCGGAGGGGCGAGCTTTGT
GGAGATGGTGGACAACCTGAGGGGCAAGTCGGGGCAGGGCTACTAC
GTGGAGATGACCGTGGGCAGCCCCCGCAGACGCTCAACATCCTGG
TGGATACAGGCAGCAGTAACTTTGCAGTGGGTGCTGCCCCCACCC
CTTCCTGCATCGCTACTACCAGAGGCAGCTGTCCAGCACATACCGGG
ACCTCCGGAAGGGTGTGTATGTGCCCTACACCCAGGGCAAGTGGGA
AGGGGAGCTGGGCACCGACCTGGTAAGCATCCCCCATGGCCCCAAC
GTCAGTGTGCGTGCCAACATTGCTGCCATCACTGAATCAGACAAGTT
CTTCATCAACGGCTCCAACCTGGGAAGGCATCCTGGGGCTGGCCTATG
CTGAGATTGCCAGGCCTGACGACTCCCTGGAGCCTTTCTTTGACTCT
CTGGTAAAGCAGACCCACGTTCCCAACCTCTTCTCCCTGCAGCTTTG
TGGTGCTGGCTTCCCCCTCAACCAGTCTGAAGTGCTGGCCTCTGTG
GAGGGAGCATGATCATTGGAGGTATCGACCACTCGCTGTACACAGGC
AGTCTCTGGTATACACCCATCCGGCGGGAGTGGTATTATGAGGTGAT
CATTGTGCGGGTGGAGATCAATGGACAGGATCTGAAAATGGACTGCA
AGGAGTACAACCTATGACAAGAGCATTGTGGACAGTGGCACCACCAAC
CTTCGTTTGCCCAAGAAAGTGTTTGAAGCTGCAGTCAAATCCATCAAG
GCAGCCTCCTCCACGGAGAAGTTCCCTGATGGTTTCTGGCTAGGAGA
GCAGCTGGTGTGCTGGCAAGCAGGCACCACCCCTTGGAACATTTTCC
CAGTCATCTCACTCTACCTAATGGGTGAGGTTACCAACCAGTCCTTCC
GCATCACCATCCTTCCGCAGCAATACCTGCGGCCAGTGGAAGATGTG
GCCACGTCCCAAGACGACTGTTACAAGTTTGCCATCTCACAGTCATC
CACGGGCACTGTTATGGGAGCTGTTATCATGGAGGGCTTCTACGTTG
TCTTTGATCGGGCCCCGAAAACGAATTGGCTTTGCTGTCAGCGCTTGC
CATGTGCACGATGAGTTCAGGACGGCAGCGGTGGAAGGCCCTTTTG
TCACCTTGGACATGGAAGACTGTGGCTACAACATTCCACAGACAGAT
GAGTCAACCCTCATGACCATAGCCTATGTCATGGCTGCCATCTGCGC
CCTCTTCATGCTGCCACTCTGCCTCATGGTGTGTCAGTGGCGCTGCC
TCCGCTGCCTGCGCCAGCAGCATGATGACTTTGCTGATGACATCTCC
CTGCTGAAG

FIG. 1A



CCATGCCGGCCCCCTCACAGCCCCGCCGGGAGCCCCGAGCCCCGCTGCCCCAGG
CTGGCCGCGCGSGTGCCGATGTAGCGGGCTCCGGATCCCAGCCTCTCCCCCT
GCTCCCGTGCTCTGCGGATCTCCCCTGACCGCTCTCCACAGCCCCGGACCCG
GGGGCTGGCCCAGGGGCCCTGCAGGCCCTGGCGTCCTGATGCCCCCAAGCT
CCCTCTCCTGAGAAGCCACCAGCACCCAGACTTGGGGGCAGGCGCCA
GGGACGGACGTGGGCCAGTGCGAGCCCAGAGGGCCCCGAAGGCCGGGGCC
CACCATGGCCCAAGCCCTGCCCTGCTCCTGCTGTGGATGGGCGCGGGAG
TGCTGCCTGCCCCACGGCACCCAGCACGGCATCCGGCTGCCCTGCGCAGC
GGCCTGGGGGGCGCCCCCTGGGGCTGCGGCTGCCCCGGGAGACCGACG
AAGAGCCCCGAGGAGCCCCGGCCGGAGGGGGCAGCTTTGTGGAGATGGTGGAC
AACCTGAGGGGGCAAGTCGGGGCAGGGCTACTACGTGGAGATGACCGTGGG
CAGCCCCCGCAGACGCTCAACATCCTGGTGGATACAGGCAGCAGTAACTT
TGCACTGGGTGCTGCCCCCACCCCTTCTGTCATCGCTACTACCAGAGGCA
GCTGTCCAGCACATACCGGGACCTCCGGAAGGGTGTGTATGTGCCCTACAC
CCAGGGCAAGTGGGAAGGGGAGCTGGGCACCGACCTGGTAAGCATCCCCC
ATGGCCCCAACGTCACTGTGCGTGCCAACATTGCTGCCATCACTGAATCAGA
CAAGTTCTTCATCAACGGCTCCAACCTGGGAAGGCATCCTGGGGCTGGCCTAT
GCTGAGATTGCCAGGCCTGACGACTCCCTGGAGCCTTTCTTTGACTCTCTGG
TAAAGCAGACCCACGTTCCCAACCTCTTCTCCCTGCAGCTTTGTGGTGCTGG
CTTCCCCCTCAACCAGTCTGAAGTGCTGGCCTCTGTGCGAGGGGAGCATGAT
CATTGGAGGTATCGACCACTCGCTGTACACAGGCAGTCTCTGGTATACACCC
ATCCGGCGGGAGTGATTATGAGGTGATCATTGTGCGGGTGAGATCAAT
GGACAGGATCTGAAAATGGAAGTCAAGGAGTACAACCTATGACAAGAGCATTG
TGGACAGTGGCACCAACCAACCTTCGTTTGCCCAAGAAAGTGTTTGAAGCTGC
AGTCAAATCCATCAAGGCAGCCTCCTCCACGGAGAAGTTCCCTGATGGTTTC
TGGCTAGGAGAGCAGCTGGTGTGCTGGCAAGCAGGCACCAACCCCTTGGAAC
ATTTTCCCAGTCATCTCACTCTACCTAATGGGTGAGGTTACCAACCAGTCCTT
CCGCATCACCATCCTTCCGCAGCAATACCTGCGGCCAGTGGAAGATGTGGC
CACGTCCCAAGACGACTGTTACAAGTTTGCCATCTCACAGTCATCCACGGGC
ACTGTTATGGGAGCTGTTATCATGGAGGGCTTCTACGTTGTCTTTGATCGGG
CCCGAAAACGAATTGGCTTTGCTGTGAGCGCTTGCCATGTGCACGATGAGTT
CAGGACGGCAGCGGTGGAAGGCCCTTTTGTACCTTGGACATGGAAGACTG
TGGCTACAACATTCCACAGACAGATGAGTCAACCCTCATGACCATAGCCTAT
GTCATGGCTGCCATCTGCGCCCTCTTCATGCTGCCACTCTGCCTCATGGTGT
GTCAGTGGCGCTGCCTCCGCTGCCTGCGCCAGCAGCATGATGACTTTGCTG
ATGACATCTCCCTGCTGAAGTGAGGAGGCCCATGGGCAGAAGATAGAGATT
CCCCTGGACCACACCTCCGTGGTTCACTTTGGTCACAAGTAGGAGACACAGA
TGGCACCTGTGGCCAGAGCACCTCAGGACCCTCCCCACCCACCAATGCCT
CTGCCTTGATGGAGAAGGAAAAGGCTGGCAAGGTGGGTTCCAGGGACTGTA
CCTGTAGGAAACAGAAAAGAGAAGAAAGAAAGCACTCTGCTGGCGGGAATAC
TCTTGGTCACCTCAAATTTAAGTCGGGAAATTCTGCTGCTTGAACTTCAGCC
CTGAACCTTTGTCCACCATTCCTTTAAATTCTCCAACCCAAAGTATTCTTCTT
TCTTAGTTTCAGAAAGTACTGGCATCACACGCAGGTTACCTTGGCGTGTGTCC
CTGTGGTACCCTGGCAGAGAAGAGACCAAGCTTGTTTCCCTGCTGGCCAAA
GTCAGTAGGAGAGGATGCACAGTTTGCTATTTGCTTTAGAGACAGGGACTGT
ATAACAAGCCTAACATTGGTGCAAAGATTGCCTCTTGAATT

FIG. 1B



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MAQALPWLLLWMGAGVLP AHGTQH GIRLPLRSG LGGAPLGLRL
PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPP
QTLNILVDTGSSNFAVGAAPHPFLHRY YQRQLSSTYRDLRKGVY
VPYTQGKWE GELGTDLV SIPHGPNVTVRANIAAITESDKFFINGS
NWE GILGLAYAEIARPDD SLEPFFDSL VKQTHVPNLFSLQLCGAG
FPLNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIV
RVEINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEAAVKS IK
AASSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTN
QSFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIM
EGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDC
GYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLR
QQHDDFADDISLLK

FIG. 2A



ETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPQT
LNILVDTGSSNFAVGAAPHPFLHRYRQLSSTYRDLRKG VYVP
YTQGWEGELGTDLVSIHPGPNVTVRANIAAITESDKFFINGSNW
EGILGLAYAEIARPDDSLEPFFDSL VKQTHVPNLFSLQLCGAGFP
LNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIVRV
EINGQDLKMDCKEYNYDKSIVDSGTTNLR LPPKKVFEEAAVKSIAA
SSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQ
SFRITILPQQYL RPVEDVATSQDDCYKFAISQSSTGTVMGAVIME
GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDC
GYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLR
QQHDDFADDISLLK

FIG. 2B



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MAQALPWLLLWMGAGVLP AHGTQH GIRLPLRSG LGGAPLGLRL
PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPP
QTLNILVDTGSSNFAVGAAPHPFLHRYYQRQLSSTYRDLRKG VY
VPYTQGKWE GELGTDLV SIPHGPNVTVRANIAAITESDKFFINGS
NWE GILGLAYAEIARPDDSLEPFFDSL VKQTHV PNLFSLQLCGAG
FPLNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIV
RVEINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEAAVKS IK
AASSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTN
QSFRITILPQQYL RPVEDVATSQDDCYKFAISQSSTGTVMGAVIM
EGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDC
GYNIPQTDEDYKDDDDK

FIG. 3A

ETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPPQT
LNILVDTGSSNFAVGAAPHPFLHRYYQRQLSSTYRDLRKG VYVP
YTQGKWE GELGTDLV SIPHGPNVTVRANIAAITESDKFFINGSNW
EGILGLAYAEIARPDDSLEPFFDSL VKQTHV PNLFSLQLCGAGFP
LNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIVRV
EINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEAAVKS IKAA
SSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQ
SFRITILPQQYL RPVEDVATSQDDCYKFAISQSSTGTVMGAVIME
GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDC
GYNIPQTDEDYKDDDDK

FIG. 3B



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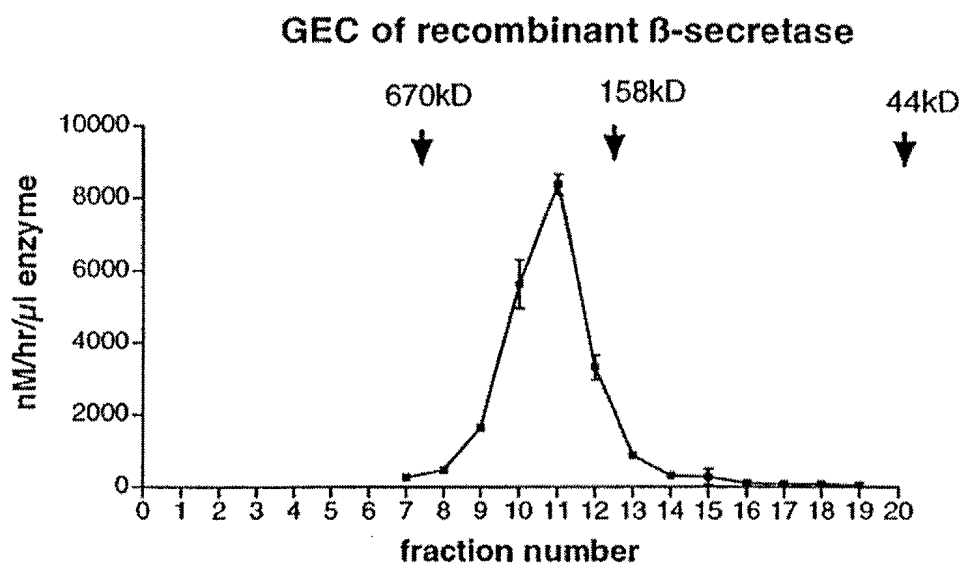
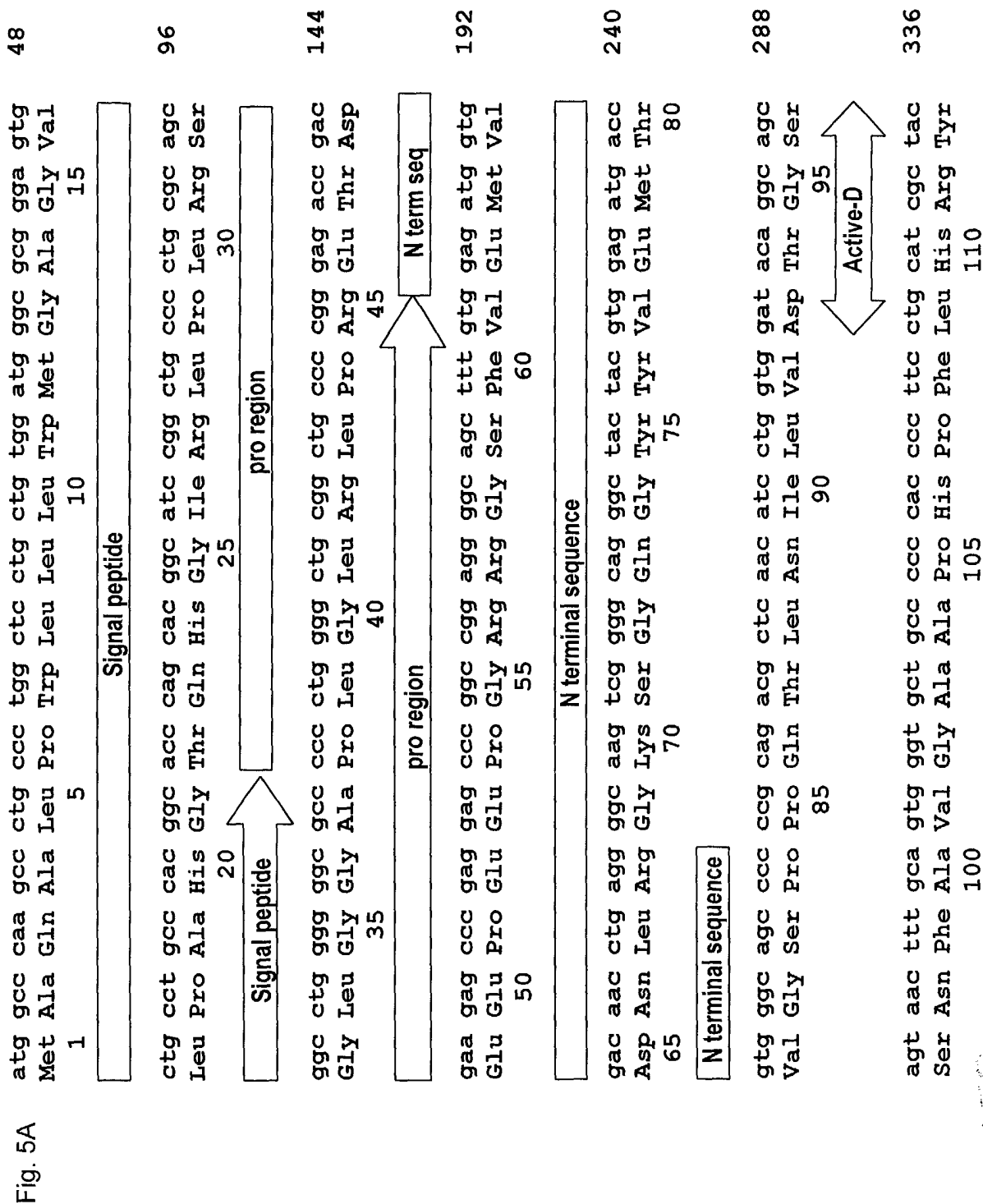


FIG. 4



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Fig. 5C

225 tct gaa gtg ctg gcc tct gtc gga ggg agc atg atc att gga ggt atc
Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
230 235 240

N-gly

768 gac cac tcg ctg tac aca ggc agt ctc tgg tat aca ccc atc cgg cgg
Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
245 250 255

816 gag tgg tat tat gag gtg atc att gtg cgg gtg gag atc aat gga cag
Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
260 265 270

864 gat ctg aaa atg gac tgc aag gag tac aac tat gac aag agc att gtg
Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
275 280 285

912 gac agt ggc acc acc aac ctt cgt ttg ccc aag aaa gtg ttt gaa gct
Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
290 295 300

Active-D

960 gca gtc aaa tcc atc aag gca gcc tcc tcc acg gag aag ttc cct gat
Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
305 310 315 320

1008 ggt ttc tgg cta gga gag cag ctg gtg tgc tgg caa gca ggc acc acc
Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
325 330 335

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Fig. 5D

cct tgg aac att ttc cca gtc atc tca ctc tac cta atg ggt gag gtt Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val	340 345 350	1056
acc aac cag tcc ttc cgc atc acc atc ctt ccg cag caa tac ctg cgg Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Tyr Leu Arg	355 360 365	1104
<div style="border: 1px solid black; padding: 2px; display: inline-block;">N-glycos</div>		
cca gtg gaa gat gtg gcc acg tcc caa gac gac tgt tac aag ttt gcc Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala	370 375 380	1152
atc tca cag tca tcc acg ggc act gtt atg gga gct gtt atc atg gag Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu	390 395 400	1200
ggc ttc tac gtt gtc ttt gat cgg gcc cga aaa cga att ggc ttt gct Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala	405 410 415	1248
gtc agc gct tgc cat gtg cac gat gag ttc agg acg gca gcg gtg gaa Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu	420 425 430	1296

Internal peptide sequence

TEVEBO

Fig. 5E

ggc cct ttt gtc acc ttg gac atg gaa gac tgt ggc tac aac att cca	1344
Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro	
435 440 445	
cag aca gat gag tca acc ctc atg acc ata gcc tat gtc atg gct gcc	1392
Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala	
450 455 460	
Transmembrane	
atc tgc gcc ctc ttc atg ctg cca ctc tgc ctc atg gtg tgt cag tgg	1440
Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp	
465 470 475 480	
Transmembrane	
cgc tgc ctc cgc tgc ctg cgc cag cag cat gat gac ttt gct gat gac	1488
Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp	
485 490 495	
atc tcc ctg ctg aag tga	1506
Ile Ser Leu Leu Lys	
500	

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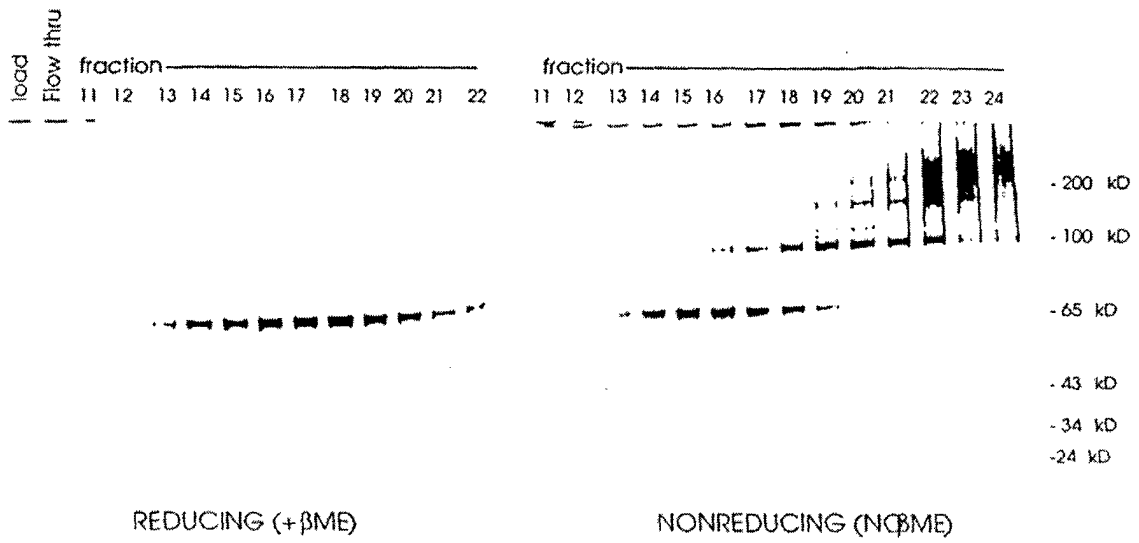


FIG. 6A

FIG. 6B

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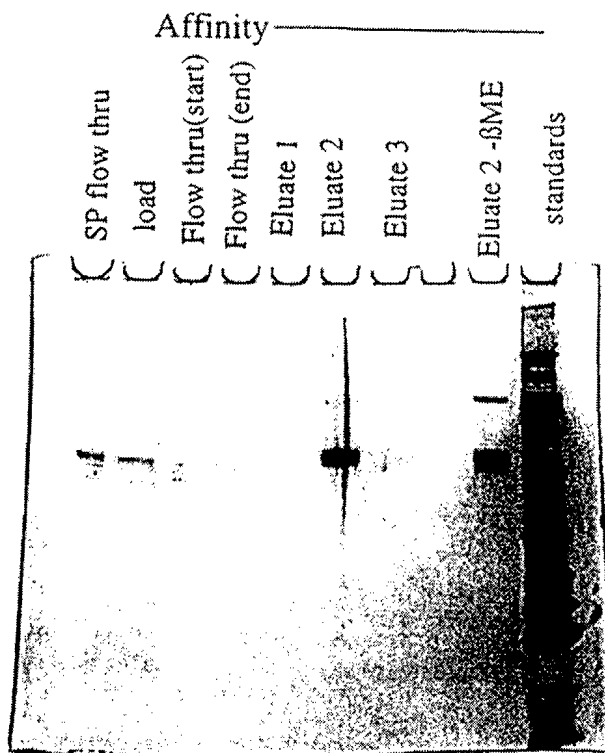


FIG. 7

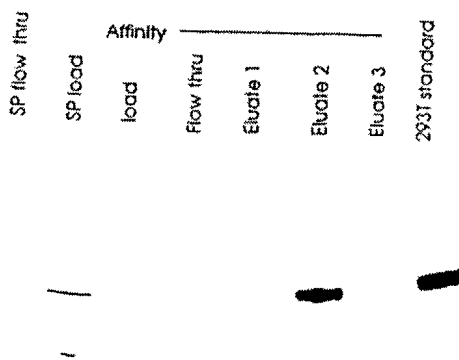


FIG. 8

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E T D E E P E E P G R R G S F V E M V D N
GARACNGAYGARGARCCNGARGARCCNGGNMGNMGNWSNTTYGTNGARATGGTNGAYAAY 63

3427-3430
5' primer set 1

3431-3434
3' primer set 1

3448-3451
5' primer set 2

3452-3455
3' primer set 2

1° HNC/primer set 1

(3428+3433)
54 bp product

1° HNC & IMR32/ primer set 2

72 bp product

sequence:

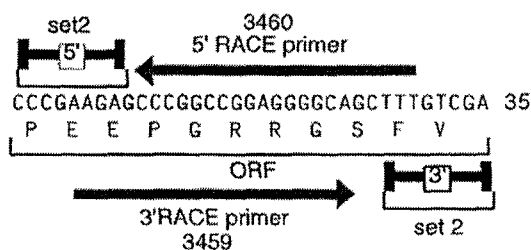


Fig. 9

SECRET

	10	20	30	40
Hump501prot	M A Q A L P W I L L W M G A G V L P A H G T Q H G I R L P L R S G L G G A P I G	40		
Musp501prot	M A P A L H W I L L W V G S G M L P A Q G T H L G I R L P L R S G L A G P P L G	40		
	50	60	70	80
Hump501prot	L R L P R E T D E E P E E P G R R G S F V E M V D N L R G K S G Q G Y Y V E M T	80		
Musp501prot	L R L P R E T D E E S E E P G R R G S F V E M V D N L R G K S G Q G Y Y V E M T	80		
	90	100	110	120
Hump501prot	V G S P P Q T L N I L V D T G S S N F A V G A A P H P F L H R Y Y Q R Q L S S T	120		
Musp501prot	V G S P P Q T L N I L V D T G S S N F A V G A A P H P F L H R Y Y Q R Q L S S T	120		
	130	140	150	160
Hump501prot	Y R D L R K G V Y V P Y T Q G K W E G E L G T D L V S I P H G P N V T V R A N I	160		
Musp501prot	Y R D L R K G V Y V P Y T Q G K W E G E L G T D L V S I P H G P N V T V R A N I	160		
	170	180	190	200
Hump501prot	A A I T E S D K F F I N G S N W E G I L G L A Y A E I A R P D D S L E P F F D S	200		
Musp501prot	A A I T E S D K F F I N G S N W E G I L G L A Y A E I A R P D D S L E P F F D S	200		
	210	220	230	240
Hump501prot	L V K Q T H Y P N I F S L Q L C G A G F P L N Q S E V L A S V G G S M I I G G I	240		
Musp501prot	L V K Q T H I P N I F S L Q L C G A G F P L N Q T E A L A S V G G S M I I G G I	240		
	250	260	270	280
Hump501prot	D H S L Y T G S L W Y T P I R R E W Y Y E V I I V R V E I N G Q D L K M D C K E	280		
Musp501prot	D H S L Y T G S L W Y T P I R R E W Y Y E V I I V R V E I N G Q D L K M D C K E	280		
	290	300	310	320
Hump501prot	Y N Y D K S I V D S G T T N L R L P K K Y F E A A V K S I K A A S S T E K F P D	320		
Musp501prot	Y N Y D K S I V D S G T T N L R L P K K Y F E A A V K S I K A A S S T E K F P D	320		
	330	340	350	360
Hump501prot	G F W L G E Q L V C W Q A G T T P W N I F P V I S L Y L M G E V T N Q S F R I T	360		
Musp501prot	G F W L G E Q L V C W Q A G T T P W N I F P V I S L Y L M G E V T N Q S F R I T	360		
	370	380	390	400
Hump501prot	I L P Q Q Y L R P V E D V A T S Q D D C Y K F A I S Q S S T G T V M G A V I M E	400		
Musp501prot	I L P Q Q Y L R P V E D V A T S Q D D C Y K F A V S Q S S T G T V M G A V I M E	400		
	410	420	430	440
Hump501prot	G F Y V V F D R A R K R I G F A V S A C H V H D E F R T A A V E G P F V T I D M	440		
Musp501prot	G F Y V V F D R A R K R I G F A V S A C H V H D E F R T A A V E G P F V T A D M	440		
	450	460	470	480
Hump501prot	E D C G Y N I P Q T D E S T L M T I A Y V M A A I C A L F M L P L C L M V C Q W	480		
Musp501prot	E D C G Y N I P Q T D E S T L M T I A Y V M A A I C A L F M L P L C L M V C Q W	480		
	490	500		
Hump501prot	R C L R C L R Q Q H D D F A D D I S L L K			
Musp501prot	R C L R C L R H Q H D D F G D D I S L L K			

501
501

FIG 10

FIG. 10

501
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CTGTTGGGCTCGCGGTTGAGGACAACTCTTCGCGGTCTTTCCAGTACTCT
TGGATCGGAAACCCGTCGGCCTCCGAACGGTACTCCGCCACCGAGGGACCT
GAGCGAGTCCGCATCGACCGGATCGGAAAACCTCTCGACTGTTGGGGTGAG
TACTCCCTCTCAAAAGCGGGCATGACTTCTGCGCTAAGATTGTCAGTTTCC
AAAAACGAGGAGGATTTGATATTCACCTGGCCCCGCGGTGATGCCTTTGAGG
GTGGCCGCGTCCATCTGGTCAGAAAAGACAATCTTTTTGTTGTCAAGCTTG
AGGTGTGGCAGGCTTGAGATCTGGCCATACACTTGAGTGACAATGACATCC
ACTTTGCCTTTCTCTCCACAGGTGTCCACTCCAGGTCCAAGTGCAGGTCTG
ACTCTAGACCC

FIG. 11A

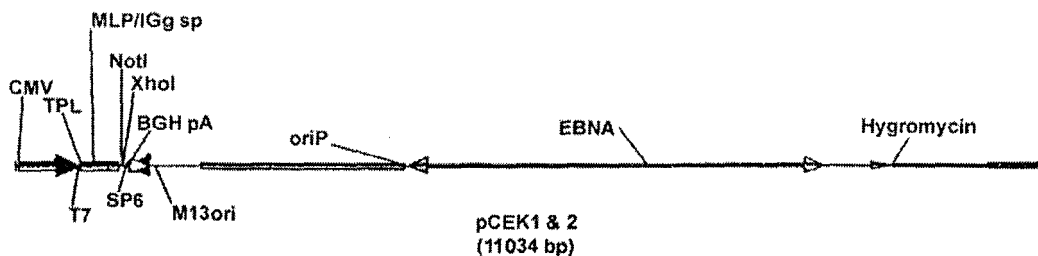


FIG. 11B

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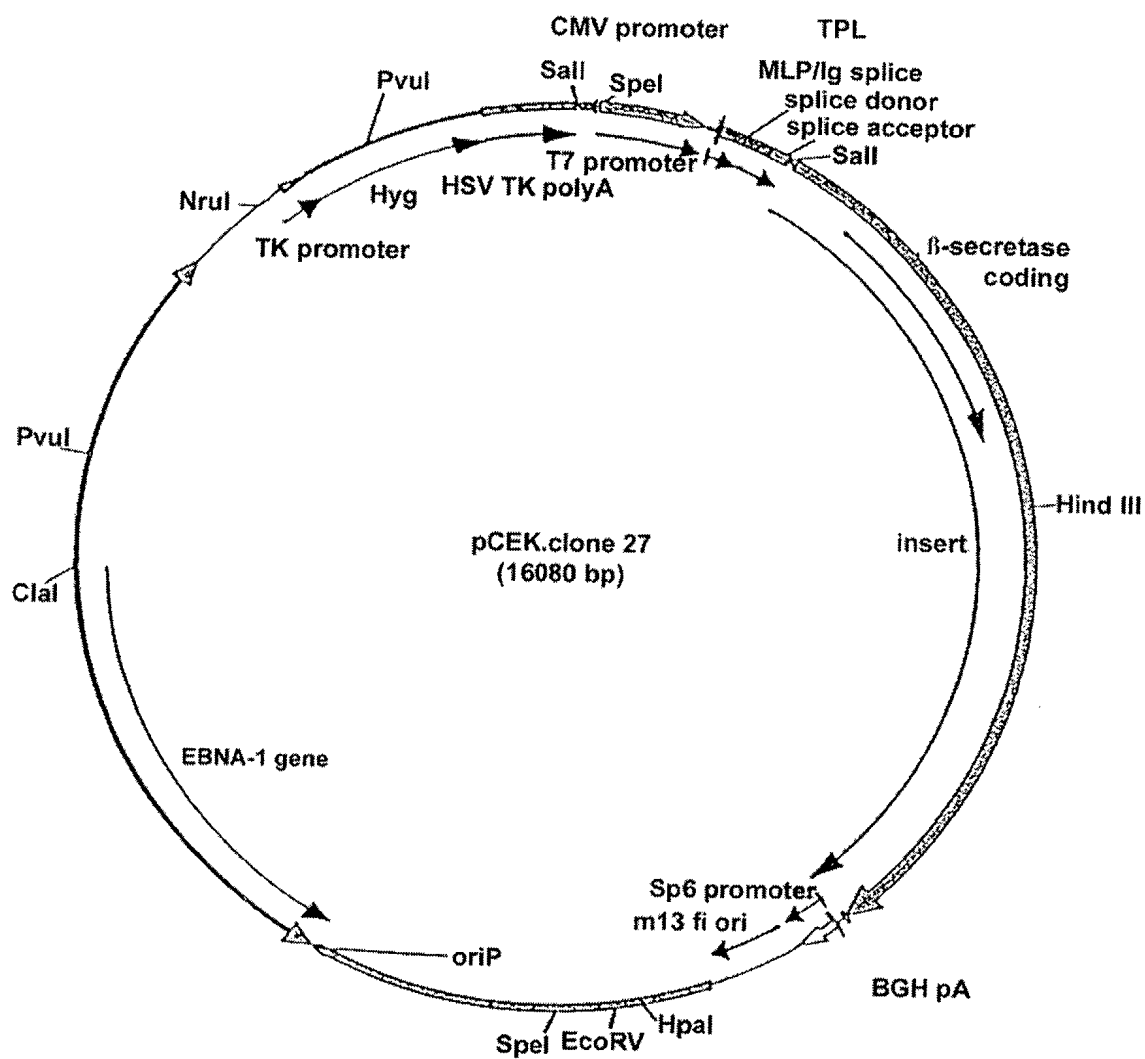


FIG. 12

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Figure 13A

ttctcatgtt tgacagctta tcatgcaga tccgggcaac gttgttgcac tgctgcaggc
gcagaaactgg taggtatgga agatccgatg tacggggccag atatacgcgt tgacattgat 120
tattgactag ttattaatag taatcaatta cgggggtcatt agttcatagc ccatatatgg 180
agttccgcgt tacataaactt acggtaaatg gccgcctgg ctgaccgccc aacgaccccc 240
gcccatggac gtcaataatg acgtatgttc ccatagtaac gccaataggg actttccatt 300
gacgtcaatg ggtggactat ttacgggtaaa ctgcccactt ggcagttacat caagtgtatc 360
atatgccaaag tacgccccct attgacgtca atgacggtaa atggcccgcc tggcattatg 420
cccagtacat gaccttatgg gactttccta ctgggcagta catctacgta ttagtcatcg 480
ctattaccat ggtgatgagg ttttggcagt acatcaatgg gcgtgggtag cggtttgact 540
cacgggggatt tccaaagtctc caccocattg acgtcaatgg gagtttgttt tggcaccaaa 600
atcaacggga ctttccaaaa tgtcgtaaca actccgcccc attgacgcaa atgggcggta 660
ggcgtgtacg gtgggagggtc tataataagca gagctctctg gctaactaga gaaccactg 720
cttactggct tatcgaaatt aatacgactc actataggga gacccaagct ctgttgggct 780

SpeI



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Figure 13B

cgcggttgag gacaaactct tcgcggtctt tccagtactc ttggatcgga aaccggtcgg 840

cctccgaacg gtactccgcc accgagggac ctgagcgagt ccgcatcgac cggatcggaa 900
splice donor

aacctctcga ctgttggggg gagtactccc tctcaaaagc gggcatgact tctgcgctaa 960

gattgtcagt ttccaaaaac gaggaggatt tgatatccac ctggccccgcg gtgatgcctt 1020

tgagggtggc cgcgtccatc tggtcagaaa agacaatctt tttgttgtca agcttgaggt 1080

gtggcaggct tgagatctgg ccatacactt ggtgacaat gacatccact ttgcctttct 1140
splice acceptor Sali

ctccacaggt gtccactccc aggtccaact gcaggtcgac tctagaccgc gggaaattctg 1200

cagatatcca tcacactggc cgcactcgtc ccagccccgc ccgggagctg cgagccgcga 1260

gctggattat ggtggcctga gcagccaacg cagccgcagg agcccgaggc ccttgccccct 1320

gcccggcgcg ccgccccgcg gggggaccag ggaagccgc accggccccgc catgccccgc 1380

cctccccagc ccgccccggg ccgcgccccg ctgcccaggc tggccgcccc cgtgccgatg 1440

tagcgggctc cggatcccag cctctccccct gctccccgtg tctgcggatc tccccgacc 1500

gctctccaca gcccggaccc gggggctggc ccagggccct gcaggccccg gcgtcctgat 1560

gcccccaagc tccctctcct gagaagccac cagcaccacc cagacttggg ggcaggcgcc 1620

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Figure 13C

aggagcggac	gtggggccagt	gcgagcccag	agggcccga	ggccggggcc	cacc	atg	1677
						Met	
						<u>1</u>	
gcc	caa	gcc	ctg	ccc	tgg	ctc	1725
Ala	Gln	Ala	Leu	Pro	Trp	Leu	
						10	
						15	
cct	gcc	cac	ggc	acc	cag	cac	1773
Pro	Ala	His	Gly	Thr	Gln	His	
						25	
						30	
ctg	ggg	ggc	ccc	ctg	ggg	ctg	1821
Leu	Gly	Gly	Ala	Pro	Leu	Gly	
						40	
						45	
gag	ccc	gag	gag	ccc	ggc	agg	1869
Glu	Pro	Glu	Glu	Pro	Gly	Arg	
						55	
						60	
						65	
aac	ctg	agg	ggc	aag	tgc	ggg	1917
Asn	Leu	Arg	Gly	Lys	Ser	Gly	
						70	
						75	
						80	
ggc	agc	ccc	ccg	cag	acg	ctc	1965
Gly	Ser	Pro	Pro	Gln	Thr	Leu	
						85	
						90	
						95	

Figure 13D

aac ttt gca gtg ggt gct gcc ccc cac ccc ttc ctg cat cgc tac tac	2013
Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr Tyr	
100 105 110	
cag agg cag ctg tcc agc aca tac cgg gac ctc cgg aag ggt gtg tat	2061
Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr	
115 120 125	
gtg ccc tac acc cag ggc aag tgg gaa ggg gag ctg ggc acc gac ctg	2109
Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Thr Asp Leu	
130 135 140 145	
gta agc atc ccc cat ggc ccc aac gtc act gtg cgt gcc aac att gct	2157
Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala	
150 155 160	
gcc atc act gaa tca gac aag ttc ttc atc aac ggc tcc aac tgg gaa	2205
Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu	
165 170 175	
ggc atc ctg ggg ctg gcc tat gct gag att gcc agg cct gac gac tcc	2253
Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser	
180 185 190	
ctg gag cct ttc ttt gac tct ctg gta aag cag acc cac gtt ccc aac	2301
Leu Glu Pro Phe Phe Asp Ser Ser Leu Val Lys Gln Thr His Val Pro Asn	
195 200 205	

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Figure 13E

ctc ttc tcc ctg cag ctt tgt ggt gct ggc ttc ccc ctc aac cag tct	2349
Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser	225
210	215
gaa gtg ctg gcc tct gtc gga ggg agc atg atc att gga ggt atc gac	2397
Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp	240
230	235
cac tcg ctg tac aca ggc agt ctc tgg tat aca ccc atc cgg cgg gag	2445
His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu	255
245	250
tgg tat tat gag gtc atc att gtg cgg gtg gag atc aat gga cag gat	2493
Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp	270
260	265
ctg aaa atg gac tgc aag gag tac aac tat gac aag agc att gtg gac	2541
Leu Lys Met Asp Cys Lys Tyr Asn Tyr Asp Lys Ser Ile Val Asp	285
275	280
agt ggc acc acc aac ctt cgt ttg ccc aag aaa gtg ttt gaa gct gca	2589
Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala	300
290	295
gtc aaa tcc atc aag gca gcc tcc tcc acg gag aag ttc cct gat ggt	2637
Val Lys Ser Ile Lys Ala Ala Ser Thr Glu Lys Phe Pro Asp Gly	315
310	320



Figure 13F

2685	ttc tgg cta gga gag cag ctg gtg tgc tgg caa gca ggc acc acc cct	325	330	335
	Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro			
2733	tgg aac att ttc cca gtc atc tca ctc tac cta atg ggt gag gtt acc	340	345	350
	Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr			
2781	aac cag tcc ttc cgc atc acc atc ctt cct cag caa tac ctg cgg cca	355	360	365
	Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro			
2829	gtg gaa gat gtg gcc acg tcc caa gac gac tgt tac aag ttt gcc atc	370	375	380
	Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile			385
2877	tca cag tca tcc acg ggc act gtt atg gga gct gtt atc atg gag ggc	390	395	400
	Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly			
2925	ttc tac gtt gtc ttt gat cgg gcc cga aaa cga att ggc ttt gct gtc	405	410	415
	Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val			
2973	agc gct tgc cat gtg cac gat gag ttc agg acg gca gcg gtg gaa ggc	420	425	430
	Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly			



Figure 13G

3021
cct ttt gtc acc ttg gac atg gaa gac tgt ggc tac aac att cca cag
Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln
435 440 445

3069
aca gat gag tca acc ctc atg acc ata gcc tat gtc atg gct gcc atc
Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ile
450 455 460 465

3117
tgc gcc ctc ttc atg ctg cca ctc tgc ctc atg gtg tgt cag tgg cgc
Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp Arg
470 475 480

3165
tgc ctc cgc tgc ctg cgc cag cag cat gat gac ttt gct gat gac atc
Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp Ile
485 490 495

3220
tcc ctg ctg aag tga ggaggcccat gggcagaaga tagagattcc cctggaccac
Ser Leu Leu Lys
500

3280
acctccgtgg ttacttttg tcacaagtag gagacacaga tggcacctgt ggccagagca

3340
cctcaggacc ctcccaccc accaaatgcc tctgccttga tggagaagga aaaggctggc

3400
aagggtgggtt ccagggactg tacctgtagg aaacagaaaa gagaagaag aagcactctg

3460
ctggcgggaa tactcttggt cacctcaaat ttaagtctgg aaattctgct gcttgaaact

Figure 13H

tcagccctga acctttgtcc accattcctt taaattctcc aacccaaagt attcttcttt 3520

tcttagtttc agaagtactg gcatcacacg caggttacct tggcgtgtgt ccctgttggt 3580

HindIII

ccctggcaga gaagagacca agcttgtttc cctgctggcc aaagtcagta ggagaggatg 3640

cacagtttgc tatttgcttt agagacaggg actgtataaa caagcctaac attggtgcaa 3700

agattgcctc ttgaattaaa aaaaaaact agattgacta tttatacaaa tggggggcggc 3760

tggaaagagg agaaggagag ggagtacaaa gacaggggat agtgggatca aagctaggaa 3820

aggcagaaac acaaccactc accagtccta gtttagacc tcatctccaa gatagcatcc 3880

catctcagaa gatgggtgtt gttttcaatg ttttctttc tgtggttgca gcctgaccaa 3940

aagtggagatg ggaagggtt atctagccaa agagctcttt tttagctctc ttaaatgaag 4000

tgcccactaa gaagttccac ttaacacatg aattctgcc atattaatt cattgtctct 4060

atctgaacca ccctttattc tacatatgat aggcagcact gaaatatacct aaccccccaa 4120

gctccagggtg ccctgtggga gagcaactgg actatagcag ggctggggtc tgtcttctctg 4180

gtcatagggt cactctttcc cccaaatctt cctctggagc ttgcagcca aggtgctaaa 4240

aggaatagggt aggagacctc ttctatctaa tccttaaaag cataatgttg aacattcatt 4300

Figure 13I

caacagctga tggcctataa cccctgcctg gatttcttcc tattaggcta taagaaagtag 4360
caagatcttt acataaattca gagtgggttc attgccttcc taccctctct aatggccctt 4420
ccatttattt gactaaagca tcacacagtg gcactagcat tataccaaga gtatgagaaa 4480
tacagtgcctt tatggctcta acattactgc cttcagtatc aaggctgcct ggagaaaagg 4540
tggcagcctc agggcttctt tatgtcctcc accacaagag ctcttgatg aaggtcattc 4600
ttttcccta tctgttctt cccctccccg ctctaattg tacgtgggtg cccaggctgg 4660
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caagccataa accaataaaa caagaatact gagtcagttt ttatatctggg ttctcttcat 4960
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caggaagact ggagactgtc cacttctagc tcggaactta ctgtgtaaat aaactttcag 5080
aactgctacc atgaagtga aatgccacat ttgctttat aatttctacc catgttgga 5140

Figure 13J

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tccttcctgc cccaaaaatta taaactctaa gtgtaaaaa aagtcttaac aacagcttct 5320
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Figure 13K

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tcctttcgct ttcttcctt cctttctgc cagttcgcc ggctttccc gtcaagctct 6760
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Figure 13L

acttgattag ggtgatggtt cacgtagtgg gccatcgccc tgatagacgg tttttcgccc 6880
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HpaI
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Figure 13M

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13M
 13M
 13M

Figure 13N

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atatgctatc ctaatctata tctgggtagc ataggctatc ctaatctata tctgggtagc 8680
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oriP

Figure 130

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ccttctgcaa tgttctcaaa tttcggggtg gaacctcctt gaccacgatg ctttccaaac 10120
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Figure 13P

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ggcctttctac ctggaggggg cctgcgcggt ggagaccgg atgatgatga ctgactactg 10360
ggactcctgg gcctcttttc tccacgtcca cgacctctcc cctgggctct ttcacgactt 10420
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cctccactac ctccctgacc cgggcctcca ctgcctctcc gaccccgcc tccacctcct 10540
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Figure 13Q

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ctgagcctca agccaggcct caaattcctc gtcccccttt ttgctggacg gtagggatgg 11800
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Figure 13R

ClaiI

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PvuI

Figure 13S

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13540-13540
13540-13540

Figure 13T

agatacctac agcgtgagct atgagaaagc gccacgcttc ccgaaggag aaagcggaac 13600
 aggtatccgg taagcggcag ggtcggaaaca ggagagcgca cgaggagct tccaggggga 13660
 aacgcctggt atctttatag tcctgtcggg ttccgccacc tctgacttga gcgtcgattt 13720
 ttgtgatgct cgtcaggggg gcggagccta tggaaaaaac ccagcaacgc ggccttttta 13780
 cggttccctgg ccttttgctg cgccgcgtgc ggctgctgga gatggcggac gcgatggata 13840
 tgttctgcc aagggttggtt tgcgcattca cagttctccg caagaattga ttggctccaa 13900
 ttcttgaggt ggtgaatccg ttagcgaggt gccgccggct tccattcagg tcgaggtggc 13960
 ccggctccat gcaccgcgac gcaacgcggg gaggcagaca aggtataggg cggcgcctac 14020
 aatccatgcc aaccggttcc atgtgctcgc cgaggcggca taaatcgccg tgacgatcag 14080
 cggtccagt atcgaagta ggctggtaag agccgcgagc gatccttga gctgtccctg 14140
 atggctcgtca tctacctgcc tggacagcat ggcctgcaac gcggggcatcc cgatgccgcc 14200
 ggaagcgaga agaatacataa tggggaaggc catccagcct cgcgctcgga acgcagcaa 14260
 gacgtagccc agcgcgtcgg ccgccatgcc ctgcttcac cccgtggccc gttgctcgcg 14320
 tttgctggcg gtgtcccccg aagaaatata tttgcatgtc tttagttcta tgatgacaca 14380

NruI

Figure 13U

aaccccgccc agcgtcttgt cattggcgaa ttcgaacacg cagatgcagt cggggcgggc 14440
cgggtcccagg tccacttcgc atattaaggt gacgcgtgtg gcctcgaaca ccgagcgacc 14500
ctgcagcgac ccgcttaaca gcgtcaacag cgtgccgcag atcccgggca atgagatatg 14560
aaaaagcctg aactcacgc gacgtctgtc gagaagtctc tgatcgaaaa gtctgcacagc 14620
gtctccgacc tgatgcagct ctcgaggggc gaagaatctc gtgctttcag ctctgatgta 14680
ggaggggcgtg gatattgtct gcgggtaaat agctgcgccg atgggtttcta caaagatcgt 14740
tagtgggac gccactttgc atcgccgcgc ctccccgatt ccggaagtgc ttgacattgg 14800
ggaattcagc gagagccctga cctattgcat ctccgcgcgt gcacaggggtg tcacgttgca 14860
agacctgcct gaaaccgaac tgcccgctgt tctgcagccg gtcgcggagg ccatggatgc 14920
PvuI
gacgcgtgcg gccgatctta gccagacgag cgggttcggc ccattcggac cgcaagggaat 14980
cgggtcaatac actacatggc gtgatttcat atgcgcgatt gctgatcccc atgtgtatca 15040
ctggcacaact gtgatggacg acaccgtcag tgcgtccgtc gcgcaggctc tcgatgagct 15100
gatgctttgg gccgaggact gcccgaagt ccggcacctc gtgcacgcgg atttcggctc 15160
caacaatgtc ctgacggaca atggccgcat aacagcgggtc attgactgga gcgagggcat 15220

Figure 13V

gttcgggggat tccaatacag aggtcgccaa catcttcttc tggaggccgt ggttgccggg 15280
tatggagcag cagacgcgct acttcgagcg gaggcatacc gagcttgacg gatcgccgcg 15340
gctccgggcg tatatgctcc gcattggtct tgaccaactc tatcagagct tggttgacgg 15400
caatttcgat gatgcagctt gggcgacagg tcgatgcgac gcaatcgtcc gatccggagc 15460
cgggactgtc gggcggtacac aaatcgcccg cagaagcgcg gccgtcttga ccgatggctg 15520
tgtagaagta ctgcccgata gtggaaacgg gagatggggg aggctaactg aaacacggaa 15580
ggagacaata ccggaaggaa cccgcgctat gacggcaata aaaagacaga ataaacgca 15640
cgggtgttgg gtcgttttgtt cataaacgcg gggttcggtc ccagggctgg cactctgtcg 15700
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accccccaag ttcgggtgaa ggcccagggc tcgcagccaa cgtcggggcg gcaggccctg 15820
ccatagccac tggccccgtg ggttagggac ggggtcccc atgggggaatg gtttatggtt 15880
cgtgggggtt attattttg gctgtgcgtg ggggtctggtc cagcactgga ctgagcagac 15940
agaccatgg tttttggatg gcctgggcat ggaccgcatg tactggcgcg acacgaacac 16000
cgggcgtctg tggctgccaa acacccccga cccccaaaa ccaccgcgcg gatttctggc 16060



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16080

Figure 13W

Sall

gtgccaaagct agtcgaccaa
▲

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CTGTTGGGCTCGCGGTTGAGGACAACTCTTCGCGGTCTTTCCAGTACTCTTGGATCGGAAAC
 CCGTCGGCCTCCGAACGGTACTCCGCCACCGAGGGACCTGAGCGAGTCCGCATCGACCGGAT
 CGGAAAACCTCTCGACTGTTGGGGTGAGTACTCCCTCTCAAAAAGCGGGCATGACTTCTGCGCT
 AAGATTGTCAGTTTCCAAAAACGAGGAGGATTTGATATTACCTGGCCCCGCGGTGATGCCTTT
 GAGGGTGGCCGCGTCCATCTGGTCAGAAAAGACAATCTTTTGTGTCAAGCTTGAGGTGTGG
 CAGGCTTGAGATCTGGCCATACACTTGAGTGACAATGACATCCACTTTGCCTTTCTCTCCACAG
 GTGTCCACTCCCAGGTCCAACCTGCAGGTGCACTCTAGACCC

FIG. 14A

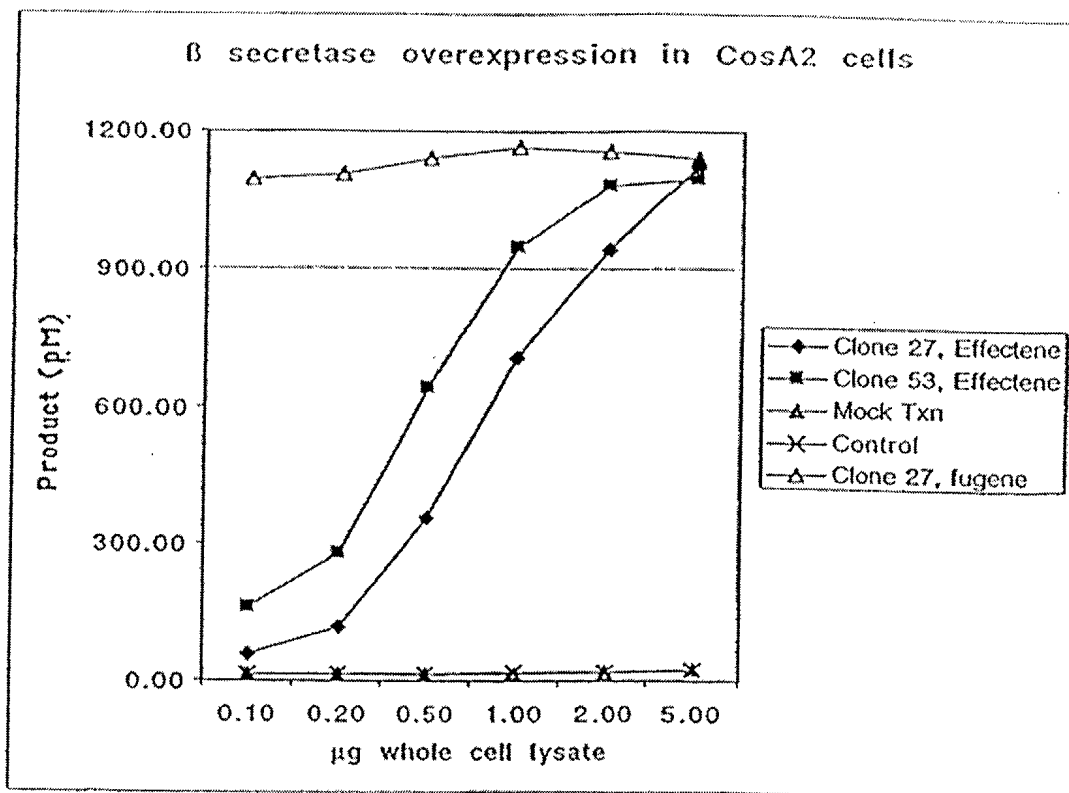


FIG. 14B



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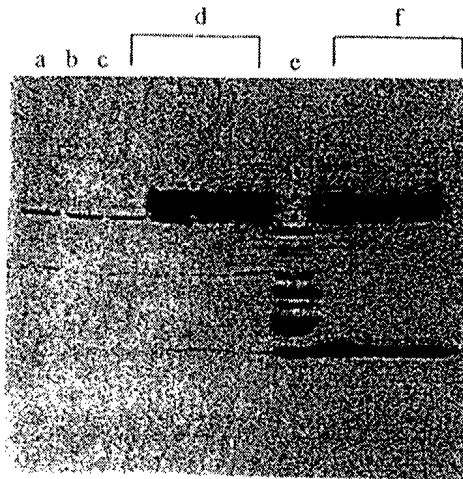


FIG. 15A

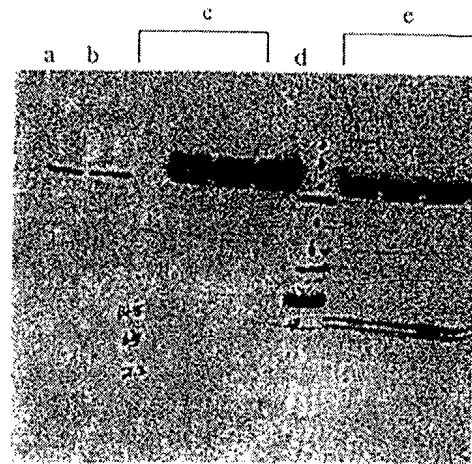


FIG. 15B

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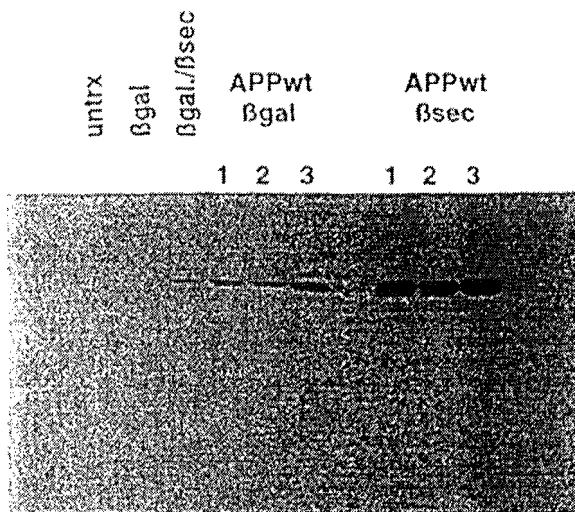


FIG. 16A

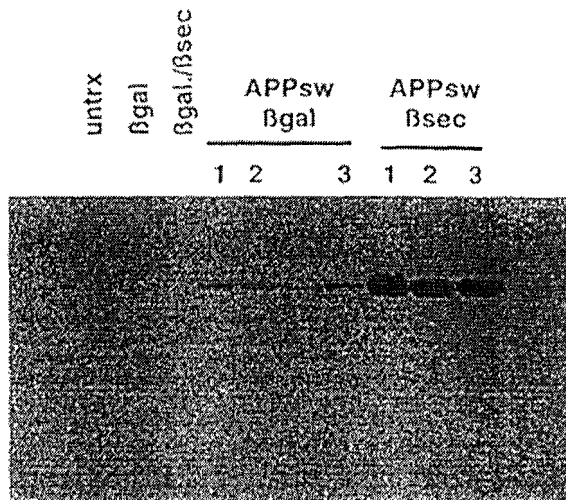


FIG. 16B

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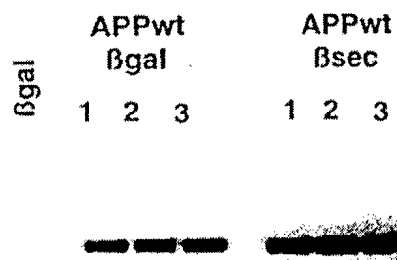


FIG. 17A

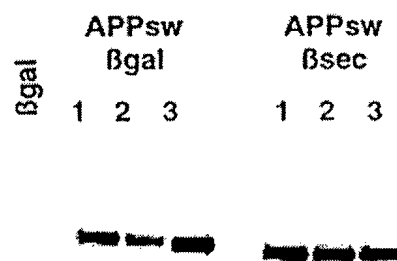


FIG. 17B

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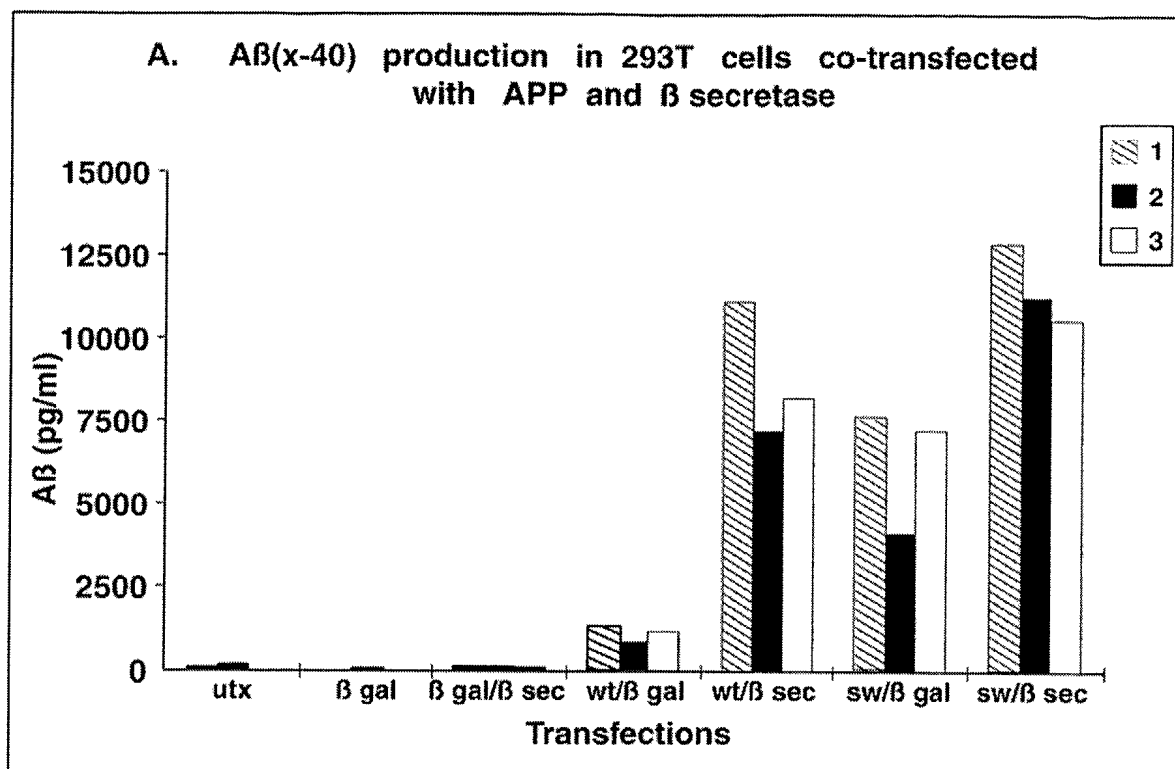


Fig. 18

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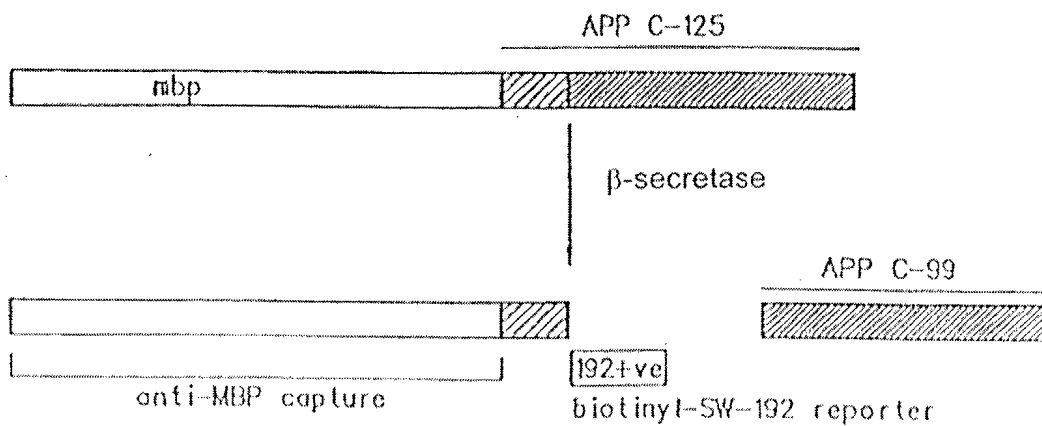


FIG. 19A

Wild-Type Sequence	...Val-Lys-Met-Asp...
Swedish Sequence	...Val-Asn-Leu-Asp...

FIG. 19B

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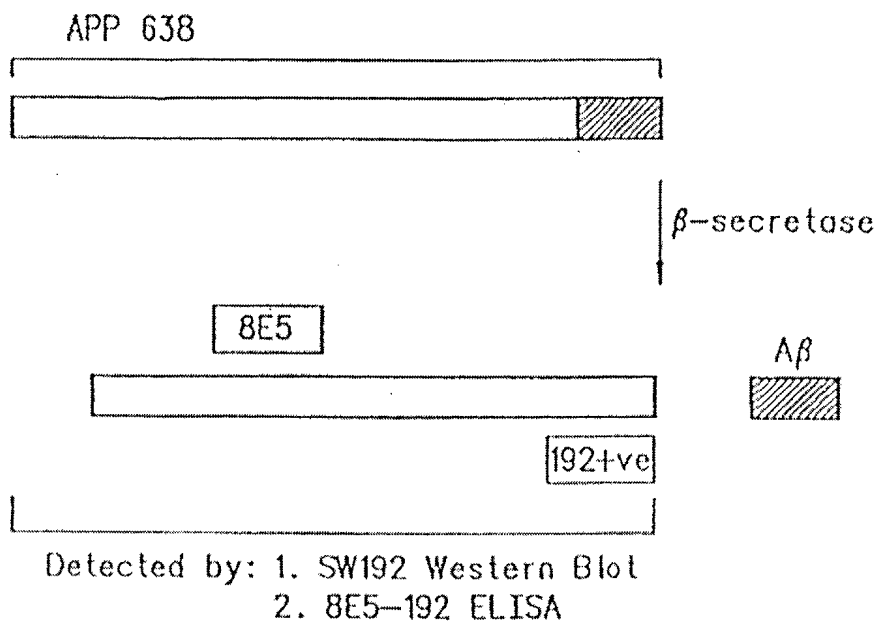


FIG. 20



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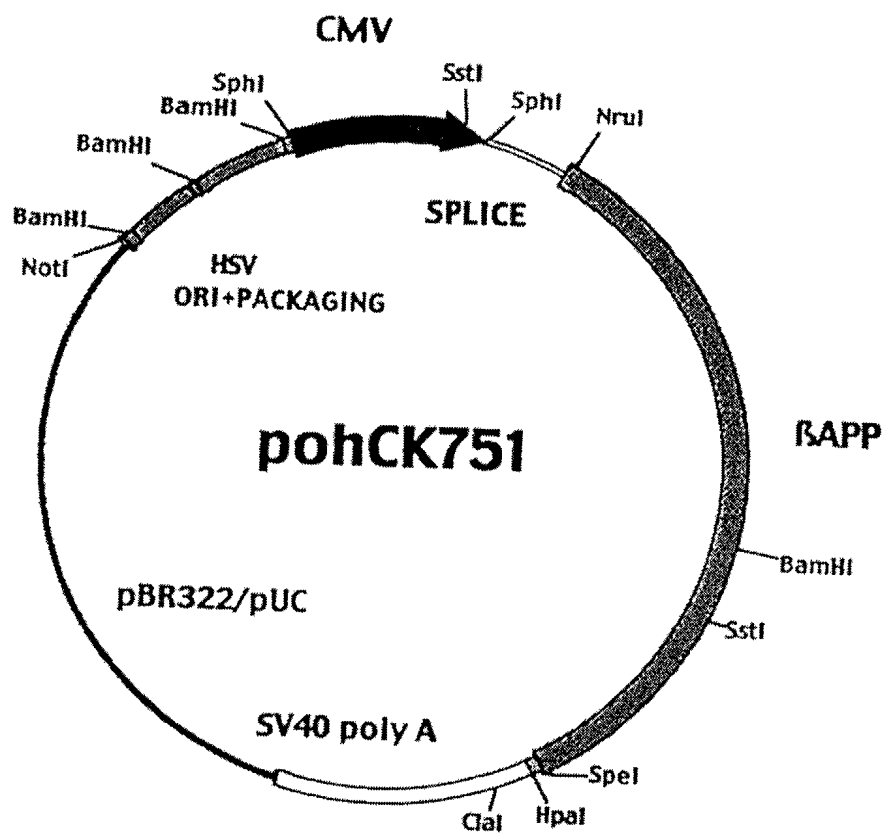


FIG. 21